

REMARKS

Claims 2-4 and 9-22 are all the claims pending in the application. Claims 1 and 5-8 have been canceled and new claims 10-22 have been added. Claims 2-4 and 9 have been amended to depend from claims 10-12 and 13-15, respectively, so that they do not depend from canceled claims. New claims 11 and 12 are claims 6 and 7 in independent form. Support for new claims 10 and 13-22 can be found, for example, in the original claims, on page 2, lines 3-11; pages 5-7; page 13, lines 6-23 and page 16, lines 3-8 of the present specification.

Initially, Applicants submit that new claims 11 and 12 are claims 6 and 7 placed in independent form. Claim 14 corresponds to claim 8 and 6, and claim 15 corresponds to claims 8 and 7. Since the Examiner has indicated on page 4 that claims 6 and 7 are allowable, Applicants submit that new claims 11-12 and 14-15 are allowable.

Claim 13 corresponds to claims 8 and 5, except *Flavimonas and Pseudomonas* are not recited. Claims 16-18 define the starting material and/or the produced material of the present invention to further distinguish the present invention. That is, claim 16 corresponds to claim 1 where the biological material is reacted with a racemic mixture of optical isomers I and II, claim 17 corresponds to claim 1 where an optically active isomer is obtained; and claim 18 corresponds to claim 8 where a biological material is reacted with a mixture of optical isomers I and II that is not a racemic mixture. Claims 19-22 depend from new claims 16-18 and correspond to claims 2, 5 (with the exception of *Flavimonas and Pseudomonas*), 6 and 7, respectively.

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Applicants respectfully submit that with the entry of the proposed amendments, the present application will be in condition for allowance. Since the amendments raise no new issues, entry of the above amendments is respectfully requested.

Applicants submit that the rejections set forth in the Office Action dated December 4, 2002 have no application to the new claims for at least the following reasons.

The present invention generally relates to a process for producing an optically active  $\alpha$ -amino acid of formula (1) by converting an enantiomer of an optically active  $\alpha$ -amino acid with a biological material, which has the ability of converting the enantiomer to the optically active  $\alpha$ -amino acid without being inhibited seriously by an amino acid transferase inhibitor. According to the present invention, an optically active amino acid is converted to its enantiomer rather than to a racemic mixture.

As discussed in the previous response, Wolfe et al. and Laiz et al. do not teach or suggest the using a specific biological material, which is not seriously inhibited by an amino acid transferase inhibitor, to convert an optical isomer of formula (1) to its enantiomer.

Wolfe et al. refers to *S. clavuligerus*, used in the purification of isopenicillin N epimerase in Example 2 bridging from the bottom of col. 7 to col. 8. In addition, from the last 2 lines of column 10 and the disclosure following, Wolfe et al. merely speculated that "substrate modified in the valinyl moiety *may be* cyclized" and "following epimerization of isopenicillin N analog to penicillin N analog", and Wolfe et al. describes that a cyclization mixture is a mixture of isopenicillin N and penicillin N.

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See col. 13, lines 26-30.

Laiz et al. refers to isopenicillin epimerase derived from *S. clavuligerus*, NRRL 3585 on page 664. Laiz et al. discloses that the reverse reaction was observed using pure preparations of penicillin N as substrate.

Although Wolfe et al. and Laiz et al. disclose epimerase, which can produce a racemic mixture of optical isomers from one optical isomer, neither reference discloses a method of converting one optical isomer of formula (1) (or a mixture that may or may not be a racemic mixture of optical isomer of formula (1) and its enantiomer) to its enantiomer, without forming a racemic mixture, as required in the present invention.

Accordingly, neither Wolfe et al. nor Laiz et al. teaches or suggests the present invention.

In addition, Lim et al. discloses an epimerization reaction as disclosed in the abstract and that the enzyme reaction showed epimerization from L- to D-allo-threonine and also from D- to L-allo-threonine. As mentioned in the previous response, the epimerized product is a mixture of an equal amount of L-threonine and D-allo-threonine. Therefore, Lim et al. does not teach or suggest the claimed process, in which a completely different enzyme is used.

Accordingly, Applicants respectfully submit that Lim et al. does not teach or suggest the present invention.

Furthermore, Hashimoto et al. discloses that L-alanine was converted to D-alanine where D-alanine formation proceeded until almost half of the L-alanine had disappeared, at which time the amount of D-alanine formed was roughly equivalent to

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the L-alanine lost. *See* right column, second paragraph on page 386. This means that a racemic mixture was formed. Therefore, Hashimoto et al. does not teach or suggest the presently claimed process, which converts an optical isomer into its enantiomer.

Gosling et al. merely refers to D-amino-acid aminotransferase and alanine racemase but no specific disclosure thereof is made.

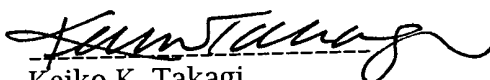
Neither Hashimoto et al. nor Gosling et al. disclose converting one optical isomer of formula (1) to its enantiomer. Therefore, Hashimoto et al. and Gosling et al. do not teach or suggest the present invention, which is not directed to racemization.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

Applicants hereby petition for any extension of time which may be required to maintain the pendency of this case, and any required fee, except for the Issue Fee, for such extension is to be charged to Deposit Account No. 19-4880.

Respectfully submitted,

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Date: April 4, 2002

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APPENDIX

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 1 and 5-8 are canceled.

The claims have been amended as follows.

2. (twice amended) The method according to Claim [1] 10, 11 or 12, wherein said optical isomer I is a D-form and said optical isomer II is a L-form.

3. (twice amended) The method according to Claim [1] 10, 11 or 12, wherein said optical isomer I with which said biological material is reacted is present in a mixture with optical isomer II.

4. (twice amended) The method according to Claim [1] 10, 11 or 12, wherein said biological material is a whole cell.

9. (amended) The method according to Claim [8] 13, 14 or 15, wherein said optical isomer I is a D-form and said optical isomer II is a L-form.

New claims 10-22 have been added.



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